April 9, 1970

Dr. Myron Tribus
Assistant Secretary of Commerce
Washington, D. C. 20230

Dear Myron:

Thank you for your letters of March 31 and April 1.
Our correspondence has so many rich issues in it that it is bound to be somewhat disorderly. If I wait to take up every question that you ask or that you provoke I will never get around to answering your letters at all, and that would be tragic.

I will, then have to include in one letter a set of very diverse questions, and hope that you also do not feel compelled to deal with all of them before answering any.

As to fluoridation (your letter of April 1) my suggestion about fluoride weeks was partly a serious proposal - but really a too gimmicky one; more importantly a satire, or, if you like, thought-experiment on the question. I am not the only critic who regrets the use of satire now and then, and I am in fact collecting a file of mea culpas of my journalistic colleagues who publish such regrets now and again. I did, however, think that exposing the situation in this way would bring most people to realize that they would not take any effort to protect themselves from a supplement of fluoride if it were delivered in the way I indicated. On the other hand, the epidemiological work that has been done on chronic fluoride exposure is probably about as good as can be managed at the present time, which means that it is basically inadequate to meet the demands of the situation.

Thank you for your comments on DENDRAL (your March 31). We have explored and often used a number of approaches to introduce efficient tree-pruning, and I suspect that our write-up is somewhat deficient in announcing all of them. We are quite sensitive to the futility of the comfpletely deterministic enumeration of the possibilities for larger molecules, and have explored a number of strategies that would at least attempt to match the performance of the human heuristics in this field. We do reach the point where human capability is equally frustrated, and have been following, mainly, two approaches.

(1) To classify the domains of confusion so that partial solutions can be expressed in terms of meaningful genera. For example, it can be anticipated that mass spectrometry will have a difficult, if not impossible, job of discriminating between isomeric alkyl chains if these are at all large. The search strategy can be simplified if we then extract the concept "alkyl", deal with it as a superatom in the system, and leave the issue of distinguishing among alkyls as a later refinement, to be pursued only if the partial solution is unacceptable and if there is some expectation that the further resolution is possible.

M. TRIBUS

(2) We also anticipate the need to call in other analytical approaches - for example, NMR, or IR. We have a paper in press now that illustrates the enormous truncation of effort that is possible when such auxiliary information is provided.

While these steps are quite essential for the efficient operation of the DENDRAL program as a chemical assistant, I have personally become rather bored with the effort of further manual refining of the system. I am instead trying to push for the construction of an executive program that will make its own tentative judgments about the organization of the search strategy and itself look for, identify, and evaluate all of the kinds of proposals for improving the program that we have been discussing. This is a meta-DENDRAL of a somewhat different character than the program that will attempt to amplify the chemical theory that is at the center of the hypothesis-evaluator.

I feel quite strongly that we have gone almost to the end of the rope in first-level programming, and that we have to learn ways of dealing with subroutines as hypotheses that need to be induced by the master program itself, perhaps roughly in the same way as hypothetical organic structures are induced by DENDRAL.

I also appreciate your note about the more systematic use of chemical stability (free energy) and I can only answer your question with the apology that we have simply never gotten around to using it more systematically, although recognizing the advantage of it. I will look for the Souders Tabler that you mentioned, and it might indeed be quite useful to us. We have used this approach in a rather ad hoc way in a few places, but have never put.together the complete table in a way that would make good sense.

Sincerely yours,

Joshua Lederberg
Professor of Genetics